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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/574,461	11/30/1995	ANTHONY D. BARONE	16528X-0155-	6825

28315 7590 07/09/2003

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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	51

DATE MAILED: 07/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
08/574,461	Barone et al
Examiner	**Art Unit**
Padmashri Ponnaluri	1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 16, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-8, 10-15, and 37-56* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-8, 10-15, and 37-56* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 50
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. A request for continued examination under 37 CAR 1.114, including the fee set forth in 37 CAR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CAR 1.114, and the fee set forth in 37 CAR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CAR 1.114. Applicant's submission filed on 4/16/03 has been entered.

2. The amendment filed on 4/16/03 has been fully considered and entered into the application.

3. Claims 1-8, 10-15, and 37-56 are currently pending and are being examined in this application.

4. Previous rejections of claims (of record) have been withdrawn in view of the amendments to the claims.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-7, 10, 12-15, 37-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claims briefly recite a method of monitoring **polymer array synthesis** (Note the polymers of claims 1-8, 10-15, 37-39 include only peptides, oligonucleotidies and carbohydrates). The polymers in the instant claims encompass a genus of polymers that is indefinitely large and includes libraries of: carbohydrates, polyolefins, polysulofones, polyureas, polycarbonates etc.

The instant specification description is directed to peptide (polymers) and nucleotide (polymers) libraries which do not provide adequate representation of the claimed method of preparing the genus nor representative of a substantial portion of the claimed genus.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound or method which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s).

In the present instance, the claimed invention contains no identifying characteristics polymers prepared by the claimed method. The specification does not describe 'structural features common to the members of the genus, which features constitute a substantial portion of the genus.

The specification description of *peptide array* and *oligonucleotide array* is not representative of the claimed genus 'polymers'. The specification does not sufficiently teach methods for preparing any other types of arrays, i.e., how to link them to the support using cleavable linkers or how to label these polymers, or how to prepare these oligomers by adding one monomer at a time and using the protecting and deprotecting steps. Further, the claimed genus encompasses diverse polymer libraries which are yet to be prepared or envisioned, which further evidences that the disclosed structural features of libraries (they are polymers made of monomers) do not constitute support for the claimed genus or a substantial portion of the claimed genus. Thus, peptide array or oligonucleotide array do not represent a substantial portion of the claimed genus. The specification does not attempt to describe the structural features that are common to all polymers. Therefore, the description provided by the specification does not allow a skilled artisan to visualize or recognize the identity of the members of the genus

Additionally, the narrow scope of examples directed to specific peptides or nucleic acids , are clearly not representative of the scope of array of compounds of the presently claimed invention.

7. Claims 1-7, 10, 12-15, 37-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for synthesis of spatially defined array of peptides and nucleic acids, does not reasonably provide enablement for synthesis of spatially defined array of diverse polymers such as carbohydrates, polyolefins, polysulofones, polyureas, polycarbonates etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims briefly recite a method of monitoring polymer array synthesis or measuring the effect of altering polymer array synthesis.

The disclosure teaches the synthesis and addition of a label to DNA or peptide polymer arrays, subsequent cleavage of the array and analysis of the resulting mixture of polymers wherein the individual members of the array are detected by a property of the label added. However, the preparation of arrays of diverse arrays of polymers, especially those limited length (specific number of units) and incorporation of labels into any polymer does not appear to be within the scope of reasonable experimentation.

The factors to be considered in a determination of undue experimentation are disclosed in *In re Wands,* (U.S.P.Q. 2d 1400 (CAFC 1988)). The factors to be considered include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the predictability of the art and the breadth of the claims.

A number of factors would prevent one of skill in the art from practicing the invention without undue experimentation, these are summarized as follows:

1) The specification fails to give adequate direction and guidance in the preparation of arrays of polymers commensurate in scope with "diverse polymers" as set forth in the claims. Moreover, as one must be able to control the length of the polymers in the claims to a specified number of monomers the chemistry used for preparation of many polymers (bulk homogeneous and heterogeneous catalysis) cannot be applied. Moreover, there is no teaching commensurate with the required incorporation of labels into "diverse polymers," only the incorporation of labels into peptides, and nucleotides. The chemistry of synthesis of carbohydrates or other chemical compounds is not same as the synthesis of oligonucleotide array or peptide array. Specifically the specification has no guidelines for synthesis of spatially defined array of other polymers, since in the synthesis of spatially defined array, protecting and deprotecitng groups are sued selectively. And the specification has no guidance in selection of protecting groups or the chemistry of the protecting groups used in the polymer array synthesis of polymers other than the polypeptides or oligonucleotides.

2) Applicants have failed to provide working examples that are commensurate in scope with the unlimited polymers claimed.

3) The breadth of the claims encompasses a literally any polymer such as the polyolefin, methacrylate, polycarbonates, carbohydrates, polysulfones etc.

4) The state of the prior art is such that methods of preparing polymers limited in the exact number of monomeric units is not widely practiced except in the nucleotide and peptide areas. Thus, one has to develop synthetic routes capable of limiting the exact number of monomeric units incorporated into any polymer (generally by step wise addition of monomers) and means of labeling the corresponding resulting polymers.

5) The art is inherently unpredictable because predicting a priori how to prepare any single polymer cannot be done with certainty. The situation is compounded by the necessity that the chemistry must be flexible enough to accommodate differing subunits and still result in the production of the expected member in each position of the array.

Therefore, while it is true that the level of skill in the art is high, it would require undue experimentation to make and use the invention commensurate in scope with that claimed in the absence of explicit guidance as to a means of preparing and labeling any polymer as set forth above.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-8, 10-15, and 37-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims recite 'a preselected array', it is not clear what does applicants mean by preselected array. Does applicants mean that the array has known composition of polymers ? Applicants are requested to clarify.

The instant claims 1 and 40 are drawn to a method of monitoring polymer array synthesis, however the method steps are related to measuring the efficiency of synthesizing step. And the measuring step (iii) seem to be incomplete. It is not clear how would efficiency determined by measuring the unbound or cleaved polymers without comparing with any standard methods of making array of polymers. It seems that the claimed methods are missing an essential method step.

The instant claims recite 'measuring efficiency of synthesizing step', it is not clear how does the presence of cleaved polymers would indicate the efficiency of synthesis step. Some of the polymers synthesized on the solid support may not be cleaved. The claimed method steps are incomplete and do not recite the required method steps.

The instant claims are briefly recite a method of monitoring polymer array synthesis (claims 1, 40) or measuring the effect of altering a polymer array synthesis (claims 10, 50), by synthesizing a preselected array which is spatially defined on a solid substrate, **cleaving the polymers from the support** and measuring the cleaved diverse polymers. From the claimed method steps, it is not clear how would the method of measuring the cleaved polymers would differ whether the polymers synthesized occupy spatially defined positions on a solid support or they randomly attached to the solid support prior to cleaving and measuring the cleaved polymers. Does applicants mean in the claimed method the spatial position of the polymers is being

monitored? Applicants are requested to amend the claim to clearly define the method steps and the relation to the claimed method.

Claim 2 recites the limitation "the labeled unbound polymers". There is insufficient antecedent basis for this limitation in the claim or in claim 39.

Claim 3 recites the limitation "the labeled unbound polymers". There is insufficient antecedent basis for this limitation in the claim or in claim 39.

Claim 4 recites the limitation "the labeled unbound polymers". There is insufficient antecedent basis for this limitation in the claim or in claim 39.

Claim 5 recites the limitation "the labeled unbound polymers". There is insufficient antecedent basis for this limitation in the claim or in claim 39.

Claims 10 and 50 recite'first synthesis protocol' and 'second synthesis protocol', it is not clear what does applicants mean by 'first synthesis protocol' and 'second synthesis protocol', and how are they different from each other. Further claims 12 and 52 recite that first and second synthesis protocols differ from each other by a single variation. It is not clear what is the single variation applicants are referring to. Since both first and second synthesis protocols are based on 'solid phase synthesis', it is not clear what is the variation applicants referring to.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 1 and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,472,672 (Brennan).

The instant claims briefly recite a method of monitoring polymer array synthesis.

Brennan (US Patent 5,472,672) teaches apparatus and method for polymer synthesis using arrays on a solid support. Brennan specifically teaches synthesis of an array of oligonucleotides on a solid support in a spatially defined positions (i.e., see Example 1) (refers to instant claims 1, 50 step I). The reference teaches that the oligonucleotides are cleaved from support (i.e., see column 16, line 16) (refers to the instant claims 1 and 50, step ii). Brennan teach that the homogenity of the product assayed by HPLC or capillary gel electrophoresis. Brennan teaches that eh typical yield of a 20 nanomolar scale synthesis of a 20-mer were 2.5 OD (85 micrograms) (refers to measuring the amount of cleaved polymer of the instant claims). Thus Brennan et al

monitor the polymer array synthesis. The reference clearly teaches all the limitations of the instant claims.

12. Claims 1-8, 10-15, 37-56 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,679,773 (Holmes).

The instant claims briefly recite a method of monitoring polymer array synthesis.

Holmes teaches methods for solid phase synthesis of organic molecules. Holmes et al teach use of linking groups which are useful in solid phase synthesis of high density arrays. Holmes et al teach that improvements to the coupling chemistry used in the light directed methods of VLSIPS process. Holmes in column 19 teaches the methods provides for the synthesis of polymers and determination of synthesis fidelity which occurs on a solid substrate. Holmes et al teach that the claimed method has a polymer attached to the solid support through a cleavable linker (i.e., see column 19, lines 39-48). Holmes teaches a labeled polymer is synthesized on a solid support (refers to step I) of the instant claims), and subsequent cleavage of the labeled polymer from the support and comparison with known standard provides a confirmation of synthesis fidelity (see column 19, lines 50-52) (refers to step iii) of the instant claims). Holmes et al teach that the precise method of synthesis is not critical and can be carried out by any of the solid phase methods described in general section above. Holmes et al teach the label refers to a marker which is detected by spectroscopic method (i.e., see column 20, lines 50-58) (refers to instant claims 37, 39, 41-43).

Holmes further teaches following the synthesis of the attached labeled polymer or small ligand molecule, the fidelity of synthesis can be determined by cleaving the labeled polymer or small ligand molecule from the solid support subjecting the labeled species to high performance liquid chromatography and comparing the resultant chromatogram with a chromatogram from a standard which is synthesized by alternative method (refers to instant claims 10-15, 50-56). Holmes clearly anticipates the claimed invention.

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 U. S. P. Q. 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 U. S. P. Q. 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 U. S. P. Q. 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 U. S. P. Q. 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CAR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CAR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CAR 3.73(b).

14. Claims 1-8, 10-15, 37-56 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-45 of U.S. Patent No. 6,576,425 (McGall et al). Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference claims are drawn to a method for testing oligonucleotide synthesis, the reference claim oligonucleotide read on the instant claim polymers. Thus, it be obvious to use the reference claimed method in the instant claimed process of monitoring or measuring the effect of altering polymer array synthesis.

15. No claims are allowed.

16. Applicant's arguments with respect to claims 1-8, 10-15, 37-56 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner is on ***Increased Flex Schedule*** and can normally be reached on Monday to Friday from 7.00 AM to 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
Primary Examiner
Technology Center 1600
Art Unit 1639
27 June 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER